ERBB3 and NGFR mark a distinct skeletal muscle progenitor cell in human development and hPSCs.

Journal: Nat Cell Biol

Publication Year: 2018

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PubMed link: 29255171

Funding Grants: Promoting survival and countering hypertrophy of pluripotent stem cell (PSC)-derived chondrocytes, Promoting survival and countering hypertrophy of pluripotent stem cell (PSC)-derived chondrocytes, Novel Platforms to Enhance In Vivo Delivery of Skeletal Muscle Progenitor Cells from Human Pluripotent Stem Cells, CRISPR/Cas9 nanoparticle enabled therapy for Duchenne Muscular Dystrophy in muscle stem cells, Pluripotent stem cell-derived chondrocytes for articular cartilage repair

Public Summary:
Human pluripotent stem cells (hPSCs) can be directed to differentiate into skeletal muscle progenitor cells (SMPCs). However, the myogenicity of hPSC-SMPCs relative to human fetal or adult satellite cells remains unclear. We observed that hPSC-SMPCs derived by directed differentiation are less functional in vitro and in vivo compared to human satellite cells. Using RNA sequencing, we found that the cell surface receptors ERBB3 and NGFR demarcate myogenic populations, including PAX7 progenitors in human fetal development and hPSC-SMPCs. We demonstrated that hPSC skeletal muscle is immature, but inhibition of transforming growth factor-beta signalling during differentiation improved fusion efficiency, ultrastructural organization and the expression of adult myosins. This enrichment and maturation strategy restored dystrophin in hundreds of dystrophin-deficient myofibres after engraftment of CRISPR-Cas9-corrected Duchenne muscular dystrophy human induced pluripotent stem cell-SMPCs. The work provides an in-depth characterization of human myogenesis, and identifies candidates that improve the in vivo myogenic potential of hPSC-SMPCs to levels that are equal to directly isolated human fetal muscle cells.

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